

COPD

Definition: A combination of small airway disease (obstructive bronchitis) and parenchymal destruction (emphysema) which causes airflow limitation that is not fully reversible. The disease is usually progressive and associated with an abnormal inflammatory response to noxious particles or gases.

Stage1: Mild	FEV1/FVC<0.70, FEV1> 80% predicted
Stage2: Moderate	FEV1/FVC<0.70, 50%<FEV1< 80% predicted
Stage3: Severe	FEV1/FVC<0.70, 30%<FEV1<50% predicted
Stage4: Very Severe	FEV1/FVC<0.70, FEV1 <30% predicted or FEV1<50% predicted plus chronic respiratory failure (PaO ₂ <60)

Pathologic Changes in COPD:

Inflammatory Cells: Increased macrophages, CD8 lymphocytes, B Lymphocytes, Fibroblasts, Neutrophils and Eosinophils

Proximal Airways (trachea, bronchi >2mm) – increased Goblet cells, enlarged submucosal glands, squamous metaplasia of epithelium

Peripheral Airway (Bronchioles <2mm) – airway wall thickening, peribronchial fibrosis, luminal inflammatory exudates, airway narrowing, increased inflammatory response

Lung Parenchyma (Respiratory bronchioles and Alveoli) – alveolar wall destruction, apoptosis of epithelial and endothelial cells

Centrilobular emphysema – respiratory bronchioles destroyed

Panacinar emphysema – respiratory bronchiole and alveoli destroyed

Pulmonary Vasculature – Thickening of intima, endothelial cell dysfunction, increased smooth muscle

Goals of Treatment: Relieve Symptoms, Prevent Disease Progression, Improve Exercise Tolerance, Improve Health Status, Prevent and Treat Complications, Prevent and Treat Exacerbations and Reduce Mortality

EBM for Acute Exacerbation

Definition: Worsening dyspnea, increased sputum purulence and increased sputum volume.

Type 1=Severe (all 3 symptoms), Type 2=Moderate (2 symptoms), Type 3=Mild (1 symptom)

Plus one of the following: URI in past 5 days or Fever without apparent cause or Increased wheezing or Increased cough or Increased respiratory rate or heart rate by 20% above baseline

Nearly half of discharged patients are readmitted to the hospital more than once in the following 6 months.

No reliable risk predictor models for relapse or mortality but look at the following:

For relapse (Return visit to ED within 14 days): low baseline FEV1, Low PaO₂, High PCO₂, low pH, more bronchodilator treatments in ED

For mortality: lower APACHE III score, lower BMI, older age, worse functional status, lower PaO₂/FIO₂

Criteria for Hospitalization (2004 American Thoracic Society/European Respiratory Society)

Inadequate response of symptoms to outpatient management

Marked increase in dyspnea

Inability to eat or sleep due to symptoms

Worsening hypoxemia

Changes in mental status

Inability to Care for oneself

Worsening Hypercapnia

Uncertain diagnosis

High risk comorbidities: pneumonia, cardiac arrhythmia, CHF, DM, CRF, Liver failure

Chest Radiograph can be helpful during Acute exacerbation

Spirometry Not Useful in Acute Setting for either diagnosis or assessing severity

Goal is to decrease symptoms and/or complications. None of the existing medications have been shown to modify the long-term decline in lung function.

Bronchodilators:

Central to symptomatic management.

Can be given on an as needed or regular basis to prevent or reduce symptoms and exacerbation

Long-acting bronchodilators are more effective and convenient.

Inhaled therapy is preferred.

All classes have been shown to increase exercise capacity but do not significantly change FEV1

Beta2-agonists –

Oral therapy is slower in onset and has more side effects than inhaled.

Bronchodilator effects wear-off in 4-6 hours in short-acting agonists.

Long-acting agonists have no loss of effectiveness overnight or with regular use.

Can cause sinus tachycardia, exaggerated somatic tremor, hypokalemia

No association with accelerated loss of lung function or increased mortality

TORCH Trial – Evaluated salmeterol vs. placebo vs. fluticasone vs. combination therapy

Decreases exacerbation rates, improved lung function and improved health-related quality of life compared to placebo. Trend toward decrease mortality but not statistically significant.

Anticholinergics –

Possible small increase in cardiovascular events in patients treated with ipratropium, needs further investigation.

UPLIFT trial – long-term RCT – supports safety of Tiotropium. No increased risk of stroke.

The original analysis suggested a small increase risk of stroke (2 cases per 1000)

Long acting anti-cholinergics reduce the rate of COPD exacerbation and improves the effectiveness of pulmonary rehabilitation.

Nebulized version can precipitate acute glaucoma

Methylxanthines – nonselective phosphodiesterase inhibitors.

Theophylline is effective but has greater potential toxicity. All studies showing efficacy were with slow-release preparations.

Low dose theophylline reduces exacerbations

Does not increase post-bronchodilator lung function

Toxicity: Atrial and ventricular arrhythmias, grand mal seizures, risk of overdose, HA, insomnia, heartburn

Salmeterol vs. Tiotropium – 2 RCTs show greater improvement of lung function with Tiotropium and 1 RCT showed greater improvement in symptoms.

Combination Bronchodilator Therapy:

Combination of short-acting B2-agonist and anticholinergic produces greater and more sustained improvements in FEV1 than either drug alone. Does not decrease exacerbations.

Salmeterol plus Tiotropium together was evaluated in 1 RCT and showed no significant difference in exacerbations, lung function or hospitalizations when compared to tiotropium alone.

Inhaled Corticosteroid (ICS):

Conflicting data whether ICS alone decreases risk for and severity of exacerbation and whether it increases FEV1

Add for symptomatic COPD patients with FEV1<50% (Stage 3 and 4) and repeated exacerbations.

NOT for monotherapy. Not the first line drug of choice. Use with bronchodilator.

When combined with bronchodilator have greater decrease in exacerbation and slowing of symptom progression than using either agent alone.

Withdrawal can lead to exacerbation in some patients.

Do they increase risk of pneumonia?

Meta-analysis, JAMA Nov 2008, 11 DB/RCTs included.

Compared inhaled steroid with nonsteroid inhaled therapy for at least 6 months of treatment.

NO difference in 1-year all cause mortality

Statistically significant increased risk of pneumonia if on highest dose ICS, shorter duration of ICS use, lowest baseline FEV1 and combined ICS and bronchodilator therapy.

However, variability between studies and pneumonia was uncommon, poorly defined and not a predetermined endpoint.

Adverse Effects: dysphonia, skin bruising, oral candidiasis, subcapsular cataracts, possible decreased bone density

ICS and Bronchodilator:

TORCH trial: Salmeterol plus fluticasone minimally decreased mortality over three years compared to placebo. Also, improved lung function, health status and rate of exacerbations.

Systemic Glucocorticoid: Not recommended due to significant side effects and increased morbidity and mortality.

Use lowest effective dose and have objective measures of improvement.

Oxygen: improves survival and quality of life. Use if have chronic hypoxemia.

Vaccines:

Pneumococcal vaccine if Age>65 or FEV1<40%

Annual influenza vaccine

Exercise Training Programs:

Improve Exercise tolerance and quality of life. Decreases symptoms of dyspnea and fatigue. Use if GOLD Stage 2, 3, or 4.

Lung Volume Reduction Surgery

One RCT comparing LVRS vs. Maximal Medical Therapy

Overall survival advantage but marked increase in early mortality in pt with FEV1<20, DLCO<20 or homogenous changes on Chest CT

Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management and Prevention of COPD, Updated 2008